solved in EtOAc (100 mL) and washed with 1 N NaOH (25 mL) and brine (25 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to provide a colorless oil, which was used without further purification.

[0358] Crude pyranone 6 (~0.56 mmol), aldehyde 7 (117 mg, 0.68 mmol), $NaCN(OAc)_3BH$ (240 mg, 1.13 mmol), and CH_2Cl_2 (2 mL) was maintained at 23° C. for 18 h. The reaction mixture was diluted with EtOAc (20 mL) and washed with 1 N NaOH (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting residue was purified by flash column chromatography (100% EtOAc) to yield 179 mg (74%) of 8 as a viscous oil.

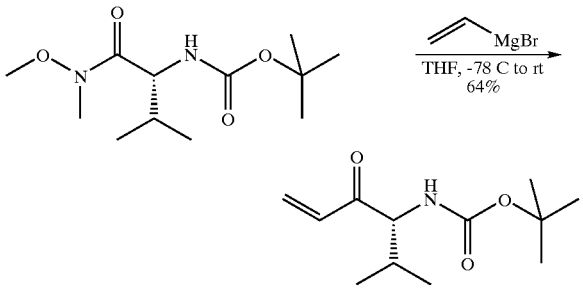
[0359] To a solution of pyranone 8 (179 mg, 0.42 mmol), diisoproylethylamine (DIEA, 0.3 mL), and CH_2Cl_2 (2 mL) at 23° C. was added p-toluoyl chloride (0.066 mL, 0.50 mmol). After 6 h, the reaction mixture was diluted with EtOAc (20 mL) and washed with saturated aqueous $NaHCO_3$ (2×5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting residue was purified by flash column chromatography (3:1 hexanes:EtOAc; 1:1 hexanes:EtOAc) to yield 100 mg (44%) of 9 as a colorless oil.

[0360] Pyanone 9 (100 mg, 0.18 mmol) and TFA:H_2O (97.5:2.5, 3 mL) was maintained at 23° C. for 1 h. The reaction mixture was concentrated. The residue was dissolved in EtOAc (20 mL) and washed with 1 N NaOH (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to provide a white solid (10) which was deemed >95% pure by ^1H NMR and LCMS analysis.

Example 2

((R)-1-Isopropyl-2-oxo-but-3-enyl)-carbamic Acid Tert-butyl Ester

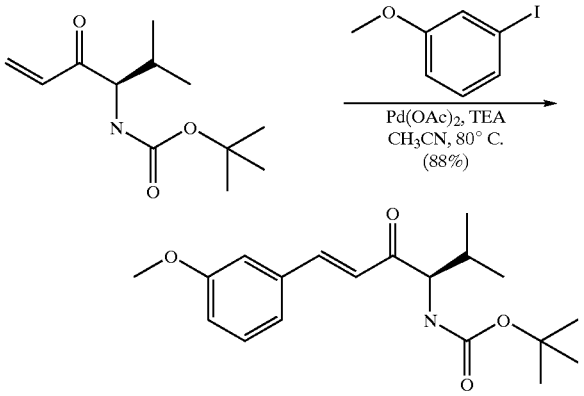
[0361]



[0362] Tetrahydrofuran (THF, 100 mL) and a 1.0M solution of vinyl magnesium bromide in THF (360 mL, 360 mmol, 3.1 equiv) was cooled to −78° C. while stirring under a nitrogen atmosphere. The mixture was treated dropwise with a solution of [(R)-(methoxy-methyl-carbamoyl)-methyl-propyl]-carbamic acid tert-butyl ester (30.3 g, 116 mmol, 1 equiv) in THF (50 mL) over 30 min. After the resultant dark yellow mixture was stirred for 30 min at −78° C., the cooling bath was removed and the reaction mixture was warmed slowly to room temperature overnight (15 h). The reaction mixture was poured slowly into an ice-chilled solution of 1N aqueous hydrochloric acid (700 mL) and then warmed to room temperature. The organics were extracted with (3×600 mL) ethyl acetate, dried over sodium sulfate, filtered, and concentrated in vacuo. Purification by flash column chromatography (5-10% ethyl acetate/hexanes) provided the product as a white solid (16.8 g, 64%). ESMS $[M+H]^+$: 228.4.

Example 3

[0363]



[(R)-(E)-1-Isopropyl-4-(3-methoxy-phenyl)-2-oxo-but-3-enyl]-carbamic Acid Tert-butyl Ester

[0364] To a solution of ((R)-1-Isopropyl-2-oxo-but-3-enyl)-carbamic acid tert-butyl ester (13.54 g, 59.6 mmol) in dry acetonitrile (150 mL) under argon, was added 3-iodoanisole (13.96 g, 59.6 mmol), triethylamine (9.1 mL, 65.6 mmol) followed by palladium (II) acetate (335 mg, 1.49 mmol). The resulting clear yellow solution was heated to 80 □C. Upon heating, the reaction darkened and the precipitation of palladium black occurred. After 15 h, the reaction mixture was allowed to cool to room temperature, quenched with water (150 mL) and diluted with ether (150 mL). The ether layer was washed with brine (100 mL) and the combined aqueous layers were extracted with ether (two 50 mL portions). The extracts were dried over magnesium sulfate, filtered and, concentrated under reduced pressure. The residue was immediately purified by silica gel chromatography (9:1 hexanes/EtOAc) to provide 17.6 g (88%) of [(R)-(E)-1-Isopropyl-4-(3-methoxy-phenyl)-2-oxo-but-3-enyl]-carbamic acid tert-butyl ester as a yellow oil. MS(ES+) m/e 334.0 $[M+H]^+$.

Example 4

[(R)-(Z)-4-(3-Cyano-phenyl)-1-isopropyl-2-oxo-but-3-enyl]-carbamic Acid Tert-butyl Ester

[0365] Following the procedure described for [(R)-(E)-1-isopropyl-4-(3-methoxy-phenyl)-2-oxo-but-3-enyl]-carbamic acid tert-butyl ester with 3-iodobenzonitrile (5.50 g, 24.0 mmol, 1 equiv) afforded the title compound as a yellow solid (7.4 g of ~90% purity material). ESMS $[M+H]^+$: 329.2.